	For receiving Office use only			
PCT	For receiving office use only			
101	International Application No.			
	International Application 10.			
REQUEST				
	International Filing Date			
The undersigned requests that the present				
international application be processed according to the Patent Cooperation Treaty.	Name of receiving Office and "PCT International Application"			
	Applicant's or agent's file reference (if desired) (12 characters maximum) PTS-0055WO			
With The Title Tit	ELLULAR-SIGNAL-REGULATED			
KINASE-6 EXPRESSION Box No. II APPLICANT This perso	n is also inventor			
No and address (F it is an a followed by given name: for a legal en	tipy full official designation. Telephone No.			
Name and address. (ramity hame followed by greatments.) The address must include postal code and name of country. The country of Box is the applicant's State (that is, country) of residence if no State of residen	the address indicated in this 760 603_2385			
•	Facsimile No.			
ISIS Pharmaceuticals Inc.	760-603-3820			
2292 Faraday Avenue Carlsbad, California 92008 US	Teleprinter No.			
Calisbad, California 52565 CC	Applicant's registration No. with the Office			
	Tippingam oregisaments			
State (that is, country) of nationality:	State (that is, country) of residence:			
US	US			
This person is applicant for the purposes of:	the United States of America the United States of America of America only the Supplemental Box			
Box No. III FURTHER APPLICANT(S) AND/OR (FURT	HER) INVENTOR(S)			
News and address (Family name followed by given name: for a legal en	tity, full official designation.			
Name and address, (ramin) manipolitowed by great must be address must include postal code and name of country. The country of Box is the applicant's State (that is, country) of residence if no State of residen	nce is indicated below.) applicant only			
	applicant and inventor			
Marcusson, Eric G.	inventor only (If this check-box			
6369 Caminito de Pastel	is marked, do not fill in below.)			
San Diego, California 92111 US	Applicant's registration No. with the Office			
State (that is, country) of nationality:	State (that is, country) of residence: US			
This person is applicant all designated or the purposes of:	ed States except States of America of America only the States indicated in the Supplemental Box			
Further applicants and/or (further) inventors are indicated	on a continuation sheet.			
Box No. IV AGENT OR COMMON REPRESENTATIVE	E; OR ADDRESS FOR CORRESPONDENCE			
The person identified below is hereby/has been appointed to act of the applicant(s) before the competent International Authorities	S 85.			
Name and address: (Family name followed by given name; for a legal en The address must include postal code and name of	tity, full official designation. Telephone No. 215-540-9200			
Bak, Mary E.	Facsimile No. 215-540-5818			
Howson and Howson Spring House Corporate Center	Teleprinter No.			
P.O. Box 457				
Spring House, Pennsylvania 19477 US	Agent's registration No. with the Office 31,215			
Address for correspondence: Mark this check-hox when	e no agent or common representative is/has been appointed and the			
space above is used instead to indicate a special address to	which correspondence should be sent.			

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Sheet	Nο		. '	-		

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)						
If none of the following sub-boxes is used, this sheet should not be included in the request.						
Name and address: (Family name followed by given name; for a legal entit The address must include postal code and name of country. The country of th Box is the applicant's State (that is, country) of residence if no State of residence	This person is:					
Bennett, C. Frank 1347 Cassins Street		applicant and inventor inventor only (If this check-box is marked, do not fill in below.)				
Carlsbad, California 92009 US	,	Applicant's registration No. with the Office				
State (that is, country) of nationality: US	State (that is, country, US	1				
for the purposes of: States the United Sta	ates of America	the United States of America only the States indicated in the Supplemental Box				
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Dobie, Kenneth W. 703 Stratford Ct., #4		inventor only (If this check-box is marked, do not fill in below.)				
Del Mar, California 92014 US		Applicant's registration No. with the Office				
State (that is, country) of nationality: UK	State (that is, country US	e) of residence:				
This person is applicant all designated the United States all designated	States except ates of America	the United States of America only the States indicated in the Supplemental Box				
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This person is applicant all designated all designated for the purposes of:	d States except lates of America	the United States of America only the Supplemental Box				
Further applicants and/or (further) inventors are indicated of						

					Sheet No3			
Во	x No.	V DESIGNATION OF STATES		М	ark the applicable check-boxes below	; at le	ast	one must be marked.
	C- 11.	owing designations are hereby made	unde	r Ru	le 4 9(a):			
			4116					•
Ke	gion	al Patent			- KE Kanua I S Lagatha MW	Mal	ฉพ	MZ Mozambique, SD Sudan,
	AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT (if other kind of protection or treatment desired, specify on dotted line).							
X	EA	Patent Convention and of the PCT	tan,	TM	Turkmenistan, and any other State w	/nicn	15 2	Contracting State of the Eurasian
X	EP	Republic, DE Germany, DK Denm IE Ireland, IT Italy, LU Luxembou TP Turkey, and any other State whi	ark, irg, ich i	EE MC	n, BG Bulgaria, CH & LI Switzerlan Estonia, ES Spain, FI Finland, FR Monaco, NL Netherlands, PT Portug Contracting State of the European Pa	rranc gal, Si itent (e, c E S Cor	Sweden, SI Slovenia, SK Slovalia, nvention and of the PCT
X		TD Chad, TG Togo, and any other of protection or treatment desired, s	toria Stat peci	al Gu e wh fy or	inea, GW Guinea-Bissau, ML Mai ich is a member State of OAPI and a a dotted line)	i, Mir Con	tra:	cting State of the PCT (if other kind
N	ation	al Patent (if other kind of protection	or	treat	ment desired, specify on dotted line):			
(32)	AF	United Arab Emirates	X	GM	Gambia			New Zealand
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	GE	Georgia	X	MZ	Mozambique	الكيا	LIV.	Zambia Zimbabwe
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P	recau	tionary Designation Statement: In	ad	ditio	n to the designations made above, the	e app	lica	int also makes under Kule 4.9(b) all

other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

Supplemental Box

If the Supplemental Box is not used, this sheet should not be included in the request.

- If, in any of the Boxes, except Boxes Nos. VIII(i) to (v) for which
 a special continuation box is provided, the space is insufficient
 to furnish all the information: in such case, write "Continuation
 of Box No..." (indicate the number of the Box) and furnish the
 information in the same manner as required according to the
 captions of the Box in which the space was insufficient, in
 particular:
- (i) if more than two persons are to be indicated as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant:
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. VI, there are more than five earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.
- If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

"Continuation of Box No. IV"

Stanley B. Kita, Reg. No. 24,561 George A. Smith, Jr., Reg. No. 24,442 Cathy A. Kodroff, Reg. 33,980 William Bak, Reg. No. 37,277 Tracy U. Palovich, Reg. No. 47,840 (patent agent)

Above attorneys are members of the firm of Howson and Howson Spring House Corporate Center P.O. Box 457 Spring House, Pennsylvania 19477 US

Herb Boswell, Reg. No. 27,311 Laurel S. Bernstein, Reg. No. 37,280 Neil S. Bartfeld, Reg. No. 39,901 Matthew Grumbling, Reg. No. 44,427 Donna T. Ward, Reg. No. 48,271

of ISIS Pharmaceuticals Inc. 2292 Faraday Avenue Carlsbad, California 92008 US

'Continuation of Box No. V" United States USSN 10/174,465 filed: 17 June 2002

USSN 10/348,431 filed: 17 January 2003

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Sheet	\1 .	_	

Box No. VI PRIORITY		SHEEL NO						
The priority of the following	g earlier application(s) is here	by claimed:						
Filing date Number Where earlier application is:								
of earlier application of earlier applic (day/month/year)		national application: country or Member of WTO	regional application:* regional Office	international application: receiving Office				
item (1) 17 June 2002	10/174,465	us		j.				
item (2) 17 January 2003	10/348,431	us						
item (3)				1				
item (4)								
item (5)								
Further priority claims	are indicated in the Supplem	ental Box.						
The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office) identified above as:								
	arching Authority (ISA) (if the Authority chosen; the two							
Request to use results of ea	arlier search; reference to							
International Searching Auth Date (day/month/year)	<i>nority):</i> Num	_	ntry (or regional Office)					
Box No. VIII DECLARA	TIONS							
The following declarations check-boxes below and indic	are contained in Boxes Nos ate in the right column the nu	. VIII (i) to (v) (mark the c mber of each type of declar	applicable ration):	Number of declarations				
Box No. VIII (i)	Declaration as to the ident	ity of the inventor		:				
Box No. VIII (ii)	Declaration as to the appl date, to apply for and be g	icant's entitlement, as at th granted a patent	ne international filing	:				
Box No. VIII (iii)	Declaration as to the app date, to claim the priority	licant's entitlement, as at to of the earlier application	the international filing	:				
Box No. VIII (iv)	Declaration of inventorsh United States of America	ip (only for the purposes o)	f the designation of the	: .				
Box No. VIII (v)	Declaration as to non-prej	judicial disclosures or exce	eptions to lack of novelty	<i>,</i> :				

Sheet No. ...6...

Box No. IX CHECK LIST; LANGUA	GE OF FII	LING						
This international application contains: (a) In paper form, the following number o sheets:	item right		Number of items					
request (including declaration sheets) :	_ `	original separate power of attorney :						
description (excluding sequence listings and/or	3. [original general power of attorney :						
sequence listings and/or tables related thereto) : 12	1	copy of general power of attorney; reference number,	4					
claims :	9	if any:	. I					
abstract .	1 5.		Ĭ					
drawings :	^{6. L}	priority document(s) identified in Box No. VI as item(s):	`					
Sub-total number of sheets: 14 sequence listings: 8	.3 7. [translation of international application into (language)::						
tables related thereto :	8. [separate indications concerning deposited microorganism or other biological material :						
(for both, actual number of sheets if filed in paper form, whether or not also filed in	9. [
computer readable form; see (c) below)	_ ((i) copy submitted for the purposes of international search under						
Total number of sheets : 23		Rule 13ter only (and not as part of the international application):						
(b) only in computer readable form (Section 801(a)(i))	- 1	ii) (only where check-box (b)(i) or (c)(i) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Rule 13ter:						
(i) sequence listings	(ii	ii) X together with relevant statement as to the identity of the copy or copies with the sequence listings mentioned in left column :	1					
(ii) ☐ tables related thereto (c) ☑ also in computer readable form	10. [tables in computer readable form related to sequence listings (indicate type and number of carriers)						
(Section 801(a)(ii)) (i) X sequence listings		(i) copy submitted for the purposes of international search under Section 802(b-quater) only (and not as part of the international						
(ii) tables related thereto	. .	application) :						
Type and number of carriers (diskette, CD-ROM, CD-R or other) on which are contained the	(1	ii) (only where check-box (b)(ii) or (c)(ii) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Section 802(b-quater):						
sequence listings: 1. diskette	(ii	ii) ogether with relevant statement as to the identity of the copy or copies with the tables mentioned in left column:						
☐ tables related thereto:	,, ,	other (specify): transmittal letter to the USRO	1					
(additional copies to be indicated under items 9(ii) and/or 10(ii), in right column)								
Figure of the drawings which should accompany the abstract:		guage of filing of the English						
BOY NO Y SIGNATURE OF APPLIC	ANT. AGI	ENT OR COMMON REPRESENTATIVE						
By:		the capacity in which the person signs (if such capacity is not obvious from reading the	request).					
	Fo	or receiving Office use only						
Date of actual receipt of the purported international application:		2. Drawing						
Corrected date of actual receipt due to la timely received papers or drawings com the purported international application:	ter but oleting							
4. Date of timely receipt of the required corrections under PCT Article 11(2):								
5. International Searching Authority (if two or more are competent): ISA								
	For I	nternational Bureau use only						
Date of receipt of the record copy by the International Bureau:								